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<p>(54) Title: ORAL HYGIENE COMPOSITION</p> <p>(57) Abstract</p> <p>An oral hygiene composition comprises an unpalatable species (such as zinc ions) and an amount of an alkali metal bicarbonate sufficient to improve the palatability of the composition in use.</p>		

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ORAL HYGIENE COMPOSITION

The present invention relates inter alia to improved oral hygiene compositions and to uses of such compositions to control dental caries and gingivitis.

5 The term "oral hygiene composition" as used herein includes inter alia dentifrices, mouthwashes, mouthsprays, toothpastes, tooth gels, toothpowders, chewing gums, lozenges and denture cleansing formulations, as well as coatings for coating or impregnating dental accessories such as dental floss, toothbrush bristles and toothpicks.

10 An important consideration in the formulation of any such composition is that of palatability, since many of the components typically used are unpalatable giving rise, for example, to sensations of astringency and bitterness.

15 Examples of astringent and bitter components include antimicrobial/antiplaque agents (such as chlorhexidine and salts thereof and cetyl pyridinium chloride), desensitising agents (such as strontium ions, potassium nitrate and potassium chloride) anticalculus/anti-plaque agents (such as zinc ions) and some surfactants.

20 US-A-4416867 (Lever Brothers) describes the problem of the astringency of zinc ions in an oral hygiene composition. The document teaches the reduction of this astringency by addition of glycerine to the composition and adjustment of pH to between 4.5 and 8.

25 EP-A-0251542 (Lion Corp) suggests the use of polyoxyethylene hydrogenated castor oil to reduce the astringency of zinc ions in an oral hygiene composition.

EP-A-0173568 (Johnson & Johnson) discusses the astringency of zinc chloride and suggests use of surfactants such as the coconut fatty acid amide of N-methyltaurine to reduce this property in an oral hygiene composition.

- 5 The use of sodium bicarbonate as an abrasive in a toothpaste, gel, or toothpowder is known. For example, GB-A-1498537 (Colgate Palmolive) describes a toothpaste containing an abrasive system comprising a minor proportion of sodium bicarbonate and a major proportion of a water-insoluble dental abrasive material compatible with the
10 sodium bicarbonate in the toothpaste.

GB-A-2137494 describes a tooth powder comprising at least 50% by weight of sodium bicarbonate particles as a dental abrasive material, wherein the sodium bicarbonate particles have a median particle size within the range of 74 to 210 microns.

- 15 GB-A-2220568 describes a dentifrice gel comprising a sodium bicarbonate abrasive (median particle size range from 10 to 200 microns) in an aqueous carrier.

- Copen ding international patent application WO 94/26244 incidentally discloses that if dentifrices containing sodium bicarbonate (i.e. with a pH of
20 about 7.5 to 9.5) comprise zinc compounds (including zinc oxide) the zinc compounds will have minimum solubility. This document states that it is surprising that zinc oxide which is insoluble still provides the desired protection, and further teaches that oral care compositions which comprise zinc oxide are less astringent or unpleasant in taste than compositions
25 comprising most other zinc salts. There is no teaching that sodium bicarbonate could be used in an oral care composition for the purpose of masking unpleasant or astringent species, indeed the document teaches away from any oral care composition comprising sodium bicarbonate in

combination with zinc compounds (other than zinc oxide) because of this stated minimum solubility of zinc compounds at high pH.

It has now surprisingly been found that alkali metal bicarbonates may be used to improve the palatability of an oral hygiene composition comprising an unpalatable species.

According to the present invention, there is provided the use of an alkali metal bicarbonate to improve the palatability of an oral hygiene composition comprising an unpalatable species, especially a bitter or astringent species.

Preferably, the alkali metal bicarbonate is sodium bicarbonate, since this has been found to give particularly good improvements in palatability.

Alkali metal bicarbonates have been found to be particularly effective when used to reduce the astringency of astringent metal ions, especially zinc ions. Suitably, therefore, the unpalatable species in the oral hygiene composition is an astringent metal ion such as zinc or strontium ions, preferably zinc ions. Zinc ions may be included in an oral hygiene composition for various reasons. For example zinc citrate may be included as an antimicrobial agent and zinc citrate or zinc chloride may be included as anti-calculus agents. The unpalatable species may also be a cationic antimicrobial agent such as chlorhexidine or cetyl pyridinium chloride.

Suitably, the alkali metal bicarbonate is used in an amount of from about 0.1% to about 95% preferably from about 0.5% to about 50%, suitably from about 0.75% to about 30% by weight of the oral hygiene composition. In a mouthwash-type composition the preferred amount is about 1% by weight and in a toothpaste/dentifrice-type composition the preferred amount is from about 0.5% to about 50% by weight.

Suitably, the concentration of alkali metal bicarbonate is between about 0.5% and about 5% by weight, more suitably between about 1% and about 4% by weight, and for example about 2% by weight of the composition. However, higher levels (for example from about 5% to about 5
60%, for example about 25%) may be employed where it is intended that the bicarbonate also functions as a thickener and/or abrasive.

Suitably, the astringent species, such as a zinc salt, preferably other than zinc oxide, is present in an amount of from about 0.1% to about 5%, preferably about 0.5% to about 2% by weight of the oral hygiene
10 composition, providing zinc ions at a concentration of from about 0.05% to about 1% by weight.

The present invention further provides an oral hygiene composition comprising an unpalatable species other than zinc oxide, especially a bitter or astringent species, and an amount of an alkali metal bicarbonate
15 sufficient to improve the palatability of the composition in use. Where the alkali metal bicarbonate is sodium bicarbonate it is preferably present in an amount of from about 0.5% to about 35% by weight of the composition, more preferably present in an amount from about 1% to about 30% by weight of composition.

20 The alkali metal bicarbonate may be either fully or partially dissolved in the composition or may be in the form of suspended particles. Suitably the bicarbonate is partly dissolved and partly in the form of suspended particles. If present such particles may, for example, have a median particle size of from about 5 to about 250 microns preferably about
25 10 to about 100 microns, for example about 40 microns. Suitably the alkali metal bicarbonate is sodium bicarbonate available as sodium bicarbonate BP from, for example, Brunner Mond and Company, UK.

Preferably, the oral hygiene compositions of the present invention comprise an alkali metal bicarbonate, preferably sodium bicarbonate and one or more of zinc citrate, zinc chloride, zinc sulphate, potassium chloride, potassium nitrate, strontium chloride, strontium acetate, chlorhexidine, and vitamins with a strong taste.

Such oral hygiene compositions may contain conventional materials such as, for example, humectants, surfactants, gelling agents, abrasives, fluoride sources, desensitising agents, flavourings, colourings, sweeteners, preservatives, structuring agents, bactericides, anti-tartar agents and anti-plaque agents.

Suitable humectants include polyhydric alcohols such as xylitol, sorbitol, glycerol, propylene glycol and polyethylene glycols. Mixtures of glycerol and sorbitol are particularly effective. A humectant helps to prevent dentifrice compositions from hardening on exposure to air, and may also provide a moist feel, smooth texture, flowability, and a desirable sweetness in the mouth. Suitably, such humectants may comprise up to about 85% by weight, preferably up to about 60% by weight of the oral hygiene composition.

Suitable surfactants are usually water-soluble organic compounds, and may be anionic, nonionic, cationic or amphoteric species. The surfactant used should preferably be reasonably stable and able to produce a foam in use.

Anionic surfactants include the water-soluble salts of C₁₀₋₁₈ alkyl sulphates (e.g. sodium lauryl sulphates), water soluble salts of C₁₀₋₁₈ ethoxylated alkyl sulphates, water soluble salts of C₁₀₋₁₈ alkyl sarcosinates, the water-soluble salts of sulphonated monoglycerides of C₁₀₋₁₈ fatty acids (e.g. sodium coconut monoglyceride sulphonates), alkyl

aryl sulphonates (e.g. sodium dodecyl benzene sulphonate) and sodium salts of the coconut fatty acid amide of N-methyltaurine.

Nonionic surfactants suitable for use in oral compositions include the products of the condensation of alkylene oxide groups with aliphatic or alkylaromatic species, and may be, for example, polyethylene oxide condensates of alkyl phenols, ethylene oxide/propylene oxide copolymers, available from BASF Wyandotte Chemical Corporation under the trade name 'Pluronic', ethylene oxide/ethylene diamine copolymers, ethylene oxide condensates of aliphatic alcohols, long chain tertiary amine oxides, long chain tertiary phosphine oxides, long chain dialkyl sulfoxides and mixtures thereof. Alternatives include ethoxylated sorbitan esters such as those available from ICI under the trade name "Tween".

Zwitterionic surfactants are generally derivatives of aliphatic quaternary ammonium, phosphonium, and sulphonium compounds, in which the aliphatic species may be branched or unbranched, and in which one of the aliphatic species is a C₈₋₁₈ species and another contains an anionic hydrophilic group, such as carboxy, sulphonate, sulphate, phosphate or orthophosphonate.

Cationic surfactants are generally quaternary ammonium compounds having one C₈₋₁₈ alkyl chain and include, for example, lauryl trimethylammonium chloride, cetyl trimethylammonium bromide, cetyl pyridinium chloride, cetyl, di-isobutylphenoxyethoxyethyl dimethylbenzylammonium chloride, coconutalkyltrimethylammonium nitrite and cetyl pyridinium fluoride. Also useful are benzyl ammonium chloride, benzyl dimethyl stearyl ammonium chloride, and tertiary amines having one C₁₋₁₈ hydrocarbon group and two (poly)oxyethylene groups.

Amphoteric surfactants are generally aliphatic secondary and tertiary amines comprising aliphatic species which may be branched or

unbranched, and in which one of the aliphatic species is a C₈₋₁₈ species and the other contains an anionic hydrophilic group, for example, sulphonate, carboxylate, sulphate, phosphonate or phosphate. Examples of quaternary ammonium compounds are the quaternized imidazole
5 derivatives available under the trade name 'Miranol' from the Miranol Chemical Company.

Suitably, the surfactant is included in an amount of up to about 20% by weight, preferably up to about 10% by weight of the oral hygiene composition.

10 Structuring agents may be required in, for example, dentifrices and gums to provide desirable textural properties and "mouthfeel". Suitable agents include natural gum binders such as gum tragacanth, xanthan gum, gum karaya and gum arabic, seaweed derivatives such as Irish moss and alginates, smectite clays such as bentonite or hectorite, carboxyvinyl
15 polymers and water-soluble cellulose derivatives such as hydroxyethyl cellulose and sodium carboxymethyl cellulose. Improved texture may also be achieved, for example, by including colloidal magnesium aluminium silicate. Suitably, the structuring agent is included in an amount of up to about 5% by weight, preferably up to about 3% by weight of the oral
20 hygiene composition.

Abrasives should preferably be capable of cleaning and/or polishing the teeth without causing harm to dental enamel or dentine. They are used most commonly in dentifrices, but may also be used in mouthwashes etc. where desired. Suitable abrasives include silica abrasives, such as
25 hydrated silicas. These include silica gels, particularly silica xerogels such as those available under the trade name 'Syloid' from W.R. Grace and Company; and also precipitated silica materials such as those available under the trade name 'Zeodent' from J.M. Huber Corporation. Also

suitable are diatomaceous earths such as those available under the trade name 'Celite' from Johns-Manville Corporation.

Alternative abrasives include alumina, insoluble metaphosphates such as insoluble sodium metaphosphate, calcium carbonate, dicalcium phosphate (in dihydrate and anhydrous forms), calcium pyrophosphate (including β -phase calcium) polymethoxylates and particulate thermosetting polymerised resins such as, for example, ureas, melamine-ureas, melamine-formaldehydes, urea-formaldehydes, melamine-urea-formaldehydes, cross-linked epoxides, melamines, phenolics, and cross-linked polyesters. Suitably, abrasives are included in an amount of up to about 80%, preferably up to about 60% by weight of the oral hygiene composition. It will be appreciated however that the alkali metal bicarbonate may itself have an abrasive function so that the presence of further abrasives may not be necessary.

Fluoride sources suitable for use in oral hygiene compositions of the present invention include sodium fluoride, zinc fluoride, potassium fluoride, aluminium fluoride, lithium fluoride, sodium monofluorophosphate, acidulated phosphate fluoride, stannous fluoride, ammonium fluoride, ammonium bifluoride and amine fluoride.

Preferably, the fluoride source is present in an amount sufficient to provide from about 50 ppm to about 4,000 ppm fluoride ions in the composition. Inclusion of a fluoride source is beneficial, since fluoride ions are known to become incorporated into the hydroxyapatite of tooth enamel, thereby increasing the resistance of the enamel to decay. Fluoride is also now thought to act locally on the tooth enamel, altering the remineralisation - demineralisation balance in favour of remineralisation. Inclusion of a fluoride source is also desirable when a polyphosphate anti-calculus agent is included, in order to inhibit the enzymic hydrolysis of such polyphosphates by salivary phosphatase enzymes.

Suitable desensitising agents include, for example, formaldehyde, potassium nitrate, potassium chloride and strontium chloride (suitably as hexahydrate), strontium acetate (suitably as hemihydrate) and sodium citrate/Pluronic gel.

- 5 Flavouring agents may be added to increase palatability and may include, for example, levo-menthol, oils of peppermint, spearmint, wintergreen, sassafras and clove. Sweetening agents may also be used, and these include D-tryptophan, saccharin, dextrose, aspartame, levulose, acesulfam, dihydrochalcones and sodium cyclamate.
- 10 Typically, such flavouring agents are included in amounts of up to about 5% by weight, preferably up to about 2% by weight of the oral hygiene composition. Colouring agents and pigments may be added to improve the visual appeal of the composition. Suitable colourants include dyes, such as FD & C blue No.1, D & C yellow No.10 and D & C yellow
- 15 No.3. A suitable and commonly used pigment is titanium dioxide, which provides a strong white colour.

- Suitably, the compositions of the invention may include an antimicrobial agent as a preservative and/or anti-plaque agent. Suitable antimicrobial agents include zinc salts such as zinc citrate, cetyl pyridinium
- 20 chloride, aliphatic amines, bis-biguanides, such as chlorhexidine, bromochlorophene, hexachlorophene, salicylanilides, quaternary ammonium compounds and triclosan. Enzymic systems providing a source of a natural biocide may be used as alternatives to or in combination with the biocides listed. For example, a system comprising
- 25 lactoperoxidase and glucose oxidase may be used to generate hydrogen peroxide in the presence of glucose, water and oxygen.

The composition may also comprise an anti-calculus agent. Suitable anti-calculus agents include polyphosphates, preferably

pyrophosphates. A preferred source of pyrophosphate is a mixture of tetrasodium pyrophosphate and tetrapotassium pyrophosphate. Suitably, the ratio of tetrasodium pyrophosphate to tetrapotassium pyrophosphate is 0:1 to 3:1, preferably 0:1 to 1:1. Preferably, tetrapotassium pyrophosphate
5 is the predominant species.

The composition may also comprise alcohol. This component is particularly useful in mouthwash formulations, where it may be used to solubilise components which have low solubility in water.

It will be appreciated that when selecting components from the list
10 above, the components chosen must be chemically and physically compatible with one another.

Particularly suitable oral compositions are those in the form of a toothpaste or liquid dentifrice. A liquid dentifrice contains components commonly associated with a paste eg abrasives, humectants and actives,
15 but the viscosity is considerably lower, and is preferably below about 50,000 cps.

The present invention further provides a method of cleansing the mouth for cosmetic purposes by oral application of a composition as defined above.

20 There is also provided a method for the treatment and/or prevention of dental caries and/or gingivitis by oral application of a composition as defined above.

There is also provided the use of a composition as defined above in the treatment and/or prevention of dental caries and/or gingivitis and the
25 use of such a composition in the manufacture of a medicament for the treatment and/or prevention of dental caries and/or gingivitis.

The nature of the present invention will be understood with reference to the following non-limiting Examples.

Example 1

A toothpaste is prepared to the following composition:

5	<u>Ingredient</u>	<u>% w/w</u>
	Sorbitol (70%)	40.00
	Sodium fluoride BP	0.24
	Silica (abrasive)	12.22
	Silica (thickener)	2.5
10	Sodium saccharin	0.26
	Sodium bicarbonate	25.00
	Sodium lauryl sulphate (available under the trade name 'Empicol LZ')	1.50
	Titanium dioxide	0.75
15	Sodium carboxymethylcellulose	0.90
	Zinc citrate trihydrate	0.50
	Sodium methyl cocoyl taurate	0.5
	Bromochlorophene	0.1
	Flavour (% by volume)	1.10
20	Purified water	to 100

Method of manufacture

1. To purified water add and dissolve sodium fluoride and sodium saccharin
2. Add sorbitol and mix thoroughly.

3. Add:-

silica (abrasive), silica (thickener), sodium carboxymethylcellulose, sodium bicarbonate, titanium dioxide, zinc citrate trihydrate, sodium lauryl sulphate and sodium methyl cocoyl taurate

5 Mix thoroughly under vacuum until smooth paste is formed.

4. Dissolve bromochlorophene in flavour oils and add this solution to the paste under vacuum.

5. Mix under vacuum until a smooth homogeneous paste is produced.

10 This formulation showed a noticeable reduction in dry aftertaste when compared to a corresponding formulation which was made up without sodium bicarbonate.

Example 2

A toothpaste is prepared to the following composition:

	<u>Ingredient</u>	<u>% w/w</u>
	Sorbitol (70%)	50.00
5	Silica (abrasive)	12.22
	Silica (thickener)	9.44
	Sodium monofluorophosphate	0.84
	Sodium saccharin	0.26
	Sodium bicarbonate	2.00
10	Sodium hydroxide BP	0.2
	Sodium lauryl sulphate (available under the trade name 'Empicol LZ')	1.50
	Titanium dioxide	0.75
	Sodium carboxymethylcellulose	0.90
15	Zinc citrate trihydrate	0.50
	Bromochlorophene	0.1
	Flavour (% by volume)	1.00
	Purified water	to 100

Method of manufacture

20 The toothpaste was prepared generally according to the method in Example 1 above.

This formulation showed a noticeable reduction in dry aftertaste when compared to a corresponding formulation which was made up without sodium bicarbonate.

Example 3

A toothpaste is prepared to the following composition:

	<u>Ingredient</u>	<u>% w/w</u>
	Sorbitol (70%)	50.00
5	Silica (abrasive)	12.22
	Silica (thickener)	8.33
	Sodium monofluorophosphate	0.84
	Sodium saccharin	0.26
	Sodium bicarbonate	2.00
10	Sodium lauryl sulphate	1.50
	Sodium hydroxide	0.20
	Titanium dioxide	0.75
	Sodium carboxymethylcellulose	0.90
	Zinc citrate trihydrate	2.00
15	Flavour (3/100) (% by volume)	1.1
	Purified water	to 100

Method of manufacture

The toothpaste was prepared generally according to the method in Example 1 above with the modification inter alia that no bromochlorophene
20 was added.

This formulation showed a noticeable reduction in dry aftertaste when compared to a corresponding formulation which was made up without sodium bicarbonate.

Claims

1. An oral hygiene composition comprising an unpalatable species other than zinc oxide and an amount of an alkali metal bicarbonate sufficient to improve the palatability of the composition in use.
- 5 2. An oral hygiene composition as claimed in claim 1, in which the alkali metal bicarbonate comprises sodium bicarbonate.
3. An oral hygiene composition as claimed in either preceding claim, in which the alkali metal bicarbonate is preferably present in an amount of from about 0.5% to about 35% by weight of the
10 composition.
4. An oral hygiene composition as claimed in any preceding claim in which the unpalatable species is selected from one or more of zinc citrate, zinc chloride, zinc sulphate, potassium chloride, potassium nitrate, strontium chloride, strontium acetate, chlorhexidine and
15 vitamins with a strong taste.
5. An oral hygiene composition as described herein with particular reference to the examples.
6. The use of an alkali metal bicarbonate to improve the palatability of an oral hygiene composition comprising an unpalatable species,
20 especially a bitter or astringent species.
7. A use of an alkali metal bicarbonate as claimed in claim 6, to improve the palatability of a composition as claimed in any of claims 1 to 5.

8. A method for the treatment or prevention of dental caries or gingivitis by oral application of a composition as claimed in any of claims 1 to 5.
9. The use of a composition as claimed in any of claims 1 to 5, in the
5 treatment and/or prevention of dental caries and/or gingivitis.
10. The use of a composition as claimed in any of claims 1 to 5, in the manufacture of a medicament for the treatment and/or prevention of dental caries and/or gingivitis.

INTERNATIONAL SEARCH REPORT

International Application No

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A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61K7/16

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US,A,4 414 203 (ALBERTO M. CABARDO, JR.) 8 November 1983 *Document*	1-10
A	US,A,4 160 022 (THOMAS J. DELANEY ET AL) 3 July 1979 *Document*	1-10
A	FR,A,2 201 865 (COLGATE-PALMOLIVE COMPANY) 3 May 1974 *Page 14, claims*	1-10
A	FR,A,2 201 866 (COLGATE-PALMOLIVE COMPANY) 3 May 1974 *Page 13: claims*	1-10

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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INTERNATIONAL SEARCH REPORT

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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A	US,A,4 623 536 (ANTHONY E. WINSTON ET AL) 18 November 1986 *Document* ---	1-10
A	PATENT ABSTRACTS OF JAPAN vol. 12, no. 472 (C-551) (3319) 9 December 1988 & JP,A,63 192 712 (NIPPON ZEORA K.K.) 10 August 1988 see abstract ---	1-10
A	GB,A,2 220 568 (CHURCH & DWIGHT) 17 January 1990 cited in the application *Page 21-24: claims* ---	1-10
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INTERNATIONAL SEARCH REPORT

Information on patent family members

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